

Linda Garmon reports from Kansas City, Mo., at the American Chemical Society meeting

Picture a penicillin right on target

When penicillins and related antibiotics are shot into the body, the targets are bacterial enzymes. Now, James R. Knox and colleagues of the University of Connecticut at Storrs have used computer and X-ray analyses to generate the first molecular-level picture of the bull's-eye on one of those targets. This research, which is described in an upcoming *SCIENCE* report, has implications for streamlining the design of new antibiotics.

The most widely used antibiotics, penicillins and cephalosporins, belong to the beta-lactam family. This particular family of drugs exerts its medicinal effect by disrupting the "cell-wall synthesizing machinery of bacteria," Knox explains. Specifically, the B-lactams inhibit enzymes that play key roles in cross-linking molecular strands into growing bacterial cell walls; inhibiting this wall-building process deforms and eventually kills the bacteria.

One enzyme involved in the wall-building process of the *Streptomyces* bacteria, D-alanyl-carboxypeptidase-transpeptidase, was the focus of the study by Knox and his cohorts, Judith A. Kelly and Paul C. Moews. The researchers first used X-ray crystallography — an analytical technique that involves beaming crystals of a sample with X-rays and collecting the resulting diffracted beams on photographic plates — to gather structural information about these large enzymes. They then allowed antibiotics to bind to the enzymes and performed another X-ray analysis. Finally, they plugged the roughly 75,000 X-ray data points obtained by these analyses into a computer to calculate a picture of this antibiotic-enzyme complex.

Researchers long have theorized that the cross-linking bacterial enzymes mistake B-lactams for chemical precursors they need to make the cell-wall network; if such were the case, B-lactams should bind to the enzymes precisely where the precursors normally do. According to the computer-generated pictures of Knox and colleagues, this is indeed the case. This confirmation of theory, along with the detailed structural information provided by the pictures, "will be invaluable" to pharmaceutical companies developing new beta-lactams, Knox says. "All of these companies have had armies of chemists using a trial-and-error approach to develop new penicillins," he says; use of the computer-generated pictures provides a more systematic method. Several companies have expressed interest in the method, and one, Squibb Institute for Medical Research in Princeton, N.J., already has asked Knox and colleagues to "take pictures" of its new beta-lactam antibiotics bound to bacterial enzymes.

Further, says Knox, "It is possible that the pictures could be used in the development of completely new families of antibiotics quite unlike the venerable beta-lactam family." These are needed, he says, because existing antibiotics are ineffective against certain strains of bacteria, and because most can be destroyed by the bacterial enzymes penicillinase and beta-lactamase before they reach their target enzymes.



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Model of target enzyme with beta-lactam antibiotic site indicated.

Quality suicide

Even in their final desperation, many people who commit suicide retain a sense of etiquette that leads them to choose an aesthetically pleasing exit over a more convenient but tacky alternative, according to a behavioral scientist at the University of California at Berkeley. The psychological dimension of suicidal behavior may help to explain the dubious distinction of the Golden Gate Bridge, a "shrine" to self-destruction that has been the site of 672 suicides since it was built nearly a half century ago. Writing in the current issue of *CRISIS: INTERNATIONAL JOURNAL OF SUICIDE AND CRISIS STUDIES*, Richard Seiden says that, based on an analysis of public records since the 1930s, the Golden Gate Bridge (connecting San Francisco with the counties north) has had five times more suicides than the Bay Bridge (which connects the city with Oakland to the east), even though the Bay Bridge has nearly twice the traffic. This statistic becomes even more striking when the addresses of the victims are considered: According to Seiden, half of the victims who lived east of the city actually crossed the Bay Bridge and drove through San Francisco in order to leap from the more famous bridge; in contrast, not a single person from north of the city has jumped from the Bay Bridge in almost 50 years. The San Francisco bridges provide a natural laboratory for suicide research, according to Seiden: Both bridges were built in the 1930s and both rise approximately 200 feet above the water. Because it permits pedestrian traffic, the Golden Gate Bridge is more accessible than the Bay Bridge; but even when pedestrian suicides were not included in the analysis, according to Seiden, the Golden Gate had three times the number of suicides. Seiden, who has been a strong advocate of suicide barriers on the Golden Gate Bridge, argues that the disproportionate rate of suicide for the bridge must be explained in terms of human suggestibility and the potency of psychological symbols. Local tourism agencies play up the suicide statistics of the landmark, he notes; but more importantly, he adds, the Golden Gate has become a symbol of death with dignity, while the bridge to Oakland is perceived as "tacky" and "declassé."

The rules of baby talk

Everybody knows that adults talk differently to infants than they do to other adults, and in recent years scientists have begun to suspect that the animated intonation of baby talk may play an important role in prelinguistic communication with very young children. New research reported in the September *DEVELOPMENTAL PSYCHOLOGY* indicates that there is indeed a pattern to the baby talk of new mothers, with unique pitch patterns being associated with different motives and emotions. Daniel N. Stern and his colleagues at the Cornell University Medical College in New York City used a sound spectroscope to analyze the intonational "contours" of six mothers' speech during interactions with their infants. They found that the mothers used distinctive tones for different kinds of sentences — declarative sentences and questions requiring a yes-or-no answer, for example. And mothers predictably used certain pitch patterns in certain contexts: they consistently raised their pitch when trying to attract a baby's attention and tended to fluctuate their pitch in a distinctive pattern when trying to maintain a baby's gaze or smile. Although there is no evidence that very young infants can appreciate the meaning of tone in baby talk (the infants in this study were less than six months old), the findings do support the idea that pitch is used to carry information about mothers' intentions and feelings, the researchers say. Other research, they note, has indicated that mothers tend to exaggerate their intonation when the infant is two months to six months old and that infants are able, by six months, to distinguish melodies and tones. Such early patterns in pitch, they suggest, might provide a rudimentary framework for later language development.